Single-Cell Analysis of Murine Long-Term Hematopoietic Stem Cells Reveals Distinct Patterns of Gene Expression during Fetal Migration.

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Public Summary:
BACKGROUND: Long-term hematopoietic stem cells (LT-HSCs) migrate from the fetal liver (FL) to the fetal bone marrow (FBM) during development. Various adhesion and chemotactic receptor genes have been implicated in the migration of adult LT-HSCs. However, their role in the migration of fetal LT-HSCs is not clearly understood due, in part, to the rare number of these cells in fetal tissues, which preclude classical gene expression analysis. The aim of this study is to characterize the expression of migration related genes in fetal LT-HSC across different anatomical locations during development. METHODOLOGY/PRINCIPAL FINDINGS: We isolated fetal LT-HSC from different developmental stages, as well as different anatomical locations, and performed single-cell multiplex RT-qPCR and flow cytometry analysis of eight molecules involved in adult LT-HSC migration. Our results show that the gene expression of the chemokine receptor Cxcr4 in LT-HSC varies across developmental microenvironments and times, while the cadherin Cdh2 (Ncad) and the calcium receptor Casr show higher gene expression and variability only in FBM at 17.5 days post coitum (dpc). The cadherin Cdh5 (Vecad) maintains high expression variability only during fetal development, while the integrin subunit Itga5 (α5) increases its variability after 14.5 dpc. The integrin subunits Itga4 (α4) and Itgal (Lfa1), as well as the selectin ligand Selplg (Psgl1), did not show differences in their expression in single LT-HSCs irrespective of the developmental times or anatomical microenvironments studied. CONCLUSIONS/SIGNIFICANCE: Our data demonstrate that the expression pattern of phenotypically identical, single LT-HSCs fluctuates as a function of developmental stage and anatomical microenvironment. This is the first exhaustive gene expression comparison of migration-related molecules in fetal tissues across developmental times, enhancing the understanding of LT-HSC migration fate decisions during development.

Scientific Abstract:
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